REMARKS

Applicants appreciate the courtesies extended by Examiners Christina Borgeest and Elizabeth Kemmerer to Allan Fanucci and Teresa Chen during a telephone interview on October 23, 2006. The comments appear herein are substantially the same as those presented and discussed during the interview.

Claims 31 and 36-42, as amended, appear in this application for the Examiner's review and consideration. Claims 31 and 40 have been amended to further define the present invention as suggested by the Examiner. Claim 95 has been amended to correct a typographical error. Claims 55, 77 and 94 have been amended to correspond to the amendments made to claim 40. Claims 32-35, 43-44, 46-49, 60-66, 68-71 and 83-86 are cancelled.

Paragraph [0116] of the published application has been amended to correct typographical errors. In particular, SEQ ID NOS: 4, 3 and 9 were recited where there should be SEQ ID NOS: 2, 1 and 10, respectively. As shown in Figure 3A-B, the native CNP1-22 is SEQ ID NO: 1 and CNP 5-22 is SEQ ID NO: 2, which is modified from CNP1-22 by the removal of the N-terminal amino acids, the ectocyclic part of the peptide. Moreover, paragraph [0115] recites that both CNP1-22 (SEQ ID NO: 1) and CNP 5-22 (SEQ ID NO: 2) yield 100% binding in the cGMP assay, which supports the amendment: "The peptide of SEQ ID NO: [[4]]2 was shown to be as active as the native CNP1-22, SEQ ID NO: [[3]]1". Furthermore, as shown in Table 2, SEQ ID NO: 10 contains a substitution of Met with Ala at amino acid position 17. This disclosure supports the amendment: "The peptide of SEQ ID NO: [[9]]10 contains a substitution of Met17 with Ala.... Furthermore, the peptide of SEQ ID NO: [[9]]10 was tested in bone culture and shown to induced elongation of Ach369 femora even at a concentration similar to that of CNP."

Process claims 45, 50-59, 67, 72-82 and 87-96 are currently withdrawn but it is understood that they will be rejoined when the product claim 31 is allowed. As no new matter is introduced, entry of the amendments at this time is warranted to reduce the issues for appeal, in particular, by placing the claims in condition for allowance.

The Examiner maintained the rejections of claims 31 and 36-42 under 35 U.S.C. §112, first paragraph, for scope of enablement. In response, Applicants have amended claim 31 to

more clearly define what the variant is. Therefore, claim 31 and its direct or indirect dependent claims 36-42 are now fully enabled.

Claim 40 was also rejected under 35 U.S.C. §112, first paragraph as failing to provide enablement for a natriuretic peptide-carrier protein fusion protein wherein the carrier protein is a "bone growth plate specific protein" and for failing to comply with the written description requirement. In response, claim 40 has been amended to replace "a bone growth plate specific protein" with "selected from the group consisting of growth hormone (GH), insulin like growth factor-1 (IGF-1) and thyroid hormone (TH)", which is fully supported by disclosures in paragraph [0122] of the published application.

Based on the foregoing, all rejections under 35 U.S.C. §112, first paragraph, should be withdrawn.

The rejection of claim 31 under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,434,133 to Tanaka et al. ("Tanaka") was maintained in the final office action. Tanaka discloses synthesis of derivatives of CNP and a vascular smooth muscle cell growth suppressing agent that contains such peptides as an effective ingredient. In particular, position H of the Tanaka peptide formula is Met or Gln. In contrast, in the currently amended claim 31, the corresponding position Xee is Ala, Trp, His, Lys, Ser or Gly, not either Met or Gln. Thus, the variant peptides of the present invention will never be identical to the Tanaka peptides. The following table further illustrates the differences between the Tanaka peptides and those of the present invention:

SEQ ID NO:5	**Xaa** Leu Ile Val	***Xbb*** Lys Leu Met	**Xcc** Leu Ile Ala Val	Asp	Arg	Ile	Gly	**Xdd** Ser Ala Gly Thr Asn	**Xee** Ala Trp His Lys Ser Gly	Ser	**Xff** Gly Lys Ala Leu	**Xgg** Leu Met
Tanaka	**D** Leu Ile Val Gly	**E** Lys Arg	**F** Leu Ile Met	Asp	Arg	Ile	Gly	***G*** Ser Ala	**H** Met Gln	Ser	Gly	Leu

Based on the foregoing, claim 31, as amended, is not anticipated by Tanaka and the rejection should be withdrawn.

The rejection of claim 31 under 35 U.S.C. §102(b) as being anticipated by a publication by Suzuki et al. (FEBS 282:321-25 (1991)) ("Suzuki") was maintained in the final office action. Suzuki relates to a high molecular weight variant of CNP isolated from cardiac atria and ventricles of European dogfish, having the peptide sequence CFGVKLDRIGA**M**SGLGC (emphasis added). In the currently amended claim 31, Xee, which corresponds to the **M** in the Suzuki sequence, is Ala, Trp, His, Lys, Ser, or Gly. Thus, claim 31, as amended, is not anticipated by Suzuki and the rejection should be withdrawn.

The rejection of claims 31 and 36-38 under 35 USC §102(b) as being anticipated by a publication by Ohbayashi et al. (*Clin. Exp. Pharma. Physiol.*, vol. 25, 986-91, 1998, referred to hereafter as "Ohbayashi") was maintained in the final office action. Ohbayashi discloses co-administration of thiorphan with administration of CNP. Since Ohbayashi does not teach any of the CNP peptide variants of the present invention, it cannot anticipate claims 31 and 36-38 and the rejection over Ohbayashi should be withdrawn.

The rejection of claim 31 under 35 USC §102(b) as being anticipated by European Patent No. EP 0528686 to Yabuta et al. (referred to hereafter as "Yabuta") was maintained in the final office action. Yabuta is directed to a process for producing a target peptide by culturing host cells transformed with an expression vector for a fusion protein of the target peptide and a protective peptide, which is a fragment of *E. coli* β-galactosidase. One of the examples of target peptides listed in Yabuta is CNP-22 which contained sequences identical to SEQ ID NO. 2. Since SEQ ID NO. 2 has been excluded in the currently amended claim 31 and Yabuta does not teach any of the other CNP variants recited in claim 31, Yabuta does not anticipate claim 31. Thus, the rejection of claim 31 over Yabuta should be withdrawn.

Accordingly, all rejections under 35 U.S.C. § 102(b) should be withdrawn.

Claims 31 and 40-42 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Yabuta, and further in view of publications by Rivera et al. (*Science* 287:826-30 (2000)) ("Rivera") and Mericq et al. (*J. Clin. Endocronol. Metab.* 85:569-73 (2000)) ("Mericq"). Applicants respectfully point out that the Examiner's comments were in error. First, with regard to the natriuretic peptide-carrier fusion protein in the present invention, it is well known in the art that a fusion protein remains intact unless cleavage events are specified. Thus, a skilled artisan will consider it superfluous to recite "a fusion protein not meant to be cleaved". Therefore, it is clear to any artisan that the fusion proteins, as recited in the claims,

are intact. Second, as explained above, Yabuta does not teach any of the CNP variants recited in the currently amended claim 31. Neither Rivera nor Merciq remedies this deficiency. Rivera discloses a novel method of controlled release of peptides such as Growth Hormone (GH) and pro-insulin by taking advantage of a conditional aggregation domain. Mericq relates to effects of growth hormone (GH) therapies in the treatment of adolescents with GH deficiency, where administration of GH with LHRH-A is compared with administration of GH alone. There was no teaching or suggestion in either Rivera or Mericq to modify CNP-22, which is disclosed in Yabuta, to achieve the CNP variants recited in claim 31 and its dependent claims 40-42. Therefore, none of the cited references, alone or in combination, discloses CNP peptide variants as recited in the currently amended claim 31 or natriuretic peptide-carrier protein fusion protein thereof as recited in claims 40-42. Thus, the rejection of claims 31 and 40-42 under 35 U.S.C. § 103(a) should be withdrawn.

In view of the above, the entire application is believed to be in condition for allowance, early notification of such would be appreciated. Should the Examiner not agree, a personal or telephonic interview is respectfully requested to discuss any remaining issues in order to expedite the eventual allowance of the claims.

Respectfully submitted,

2/8/07

Date

Allan A. Fanucci (Reg. No. 30,256)

WINSTON & STRAWN LLP
Customer No. 28765

212-294-3311